Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Clinical Virology 140 (2021) 104852

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Reduced sensitivity of SARS-CoV-2 PCR testing with single-nostril nasal swabs

To the Editors,

Nasopharyngeal (NP) specimens collected by clinicians are used as the "gold standard" for diagnostic real-time reverse transcriptase polymerase chain reaction (rRT-PCR) testing for SARS-CoV-2. Previous reports indicate that two-nostril nasal swabs offer a sensitive (94%) alternative to NP specimens and are better tolerated by patients [1]. Importantly, Food and Drug Administration (FDA) authorization of nasal swab protocols require sampling of both nostrils.

Prior to FDA authorization of two-nostril nasal swabs, we evaluated the diagnostic accuracy of single-nostril nasal swabs (used for sampling other respiratory viruses [2]) in household transmission investigations in Utah and Wisconsin during March 22–April 25, 2020 [3]. NP specimens were collected by CDC clinicians from the patient's right nostril. Single-nostril nasal swabs were collected from the left nostril by investigation participants (see Supplementary Materials). Paired specimens were collected from each participant at one or more time points during the 14-day study period; statistical positive percent agreement (PPA) and negative percent agreement (NPA) of nasal swabs compared to NP specimens were calculated using generalized estimating equations to adjust for correlation across time points. All specimens were tested for the presence of SARS-CoV-2 N1 and N2 viral RNA targets by rRT-PCR. Methods are further described in the Supplementary Materials.

We collected 452 paired NP and nasal swab specimens from 226 participants. When compared with NP specimens, single-nostril nasal swabs demonstrated a PPA of 47% (95% confidence interval [CI]:38%–57%; Fig. 1) and a NPA of 99% (95% CI: 98%–100%). Measured PPAs of single-nostril nasal swabs were similarly low at study sites in Utah (43%; 95% CI: 33%–55%) and Wisconsin (57%; 95% CI: 42%–78%). The PPA of single-nostril nasal swabs was significantly associated with rRT-PCR cycle threshold (Ct) values of the viral target in the paired NP specimens (Cochran-Armitage $p<0.001$ for the N1 target; $p=0.001$ for the N2 target). PPA of single-nostril nasal swabs was higher (78%; 95% CI: 61%–100%) among children (age range among cases: 3-17 years), lower among participants who reported no symptoms at collection (32%; 95% CI: 19%–55%), and was negatively associated with days between onset and collection (Cochran-Armitage $p<0.001$); the negative association with days between onset and collection remained significant when stratified by Ct value category. These trends reflect statistically significant trends in NP Ct values observed in this study population [4]. Further details are available in the Supplementary Materials.

Two-nostril nasal swabs produce less discomfort than NP swabs. While two-nostril nasal swabs demonstrate a sensitivity of 94% [1], our analysis indicates that single-nostril nasal swabs demonstrate a low PPA of 47% and that the PPA of single-nostril swabs is lowest (32%) among persons with Ct values over 30 (low levels of viral RNA, suggesting low viral burden). This discrepancy might be related to sampling variability between nostrils, as has been observed for influenza A virus [5]. As a result, single-nostril nasal swabs are likely to result in a high proportion of false-negative results leading to missed cases and, potentially, increased transmission. The distinction between single-nostril and two-nostril swabs is critical as many clinicians, familiar with single-nostril nasal swab sampling protocols for other respiratory viruses [2], might perform single-nostril nasal swabs when sampling for SARS-CoV-2. Additionally, it is critical to ensure patients are reminded and understand the importance of swabbing both nostrils when conducting self-collected nasal swabs. Our results reinforce the importance of proper specimen collection technique and sampling of both nostrils to ensure accurate testing results.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention (CDC).

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcv.2021.104852.

https://doi.org/10.1016/j.jcv.2021.104852
Received 12 February 2021; Received in revised form 16 April 2021; Accepted 1 May 2021
Available online 9 May 2021
1386-6532/Published by Elsevier B.V.

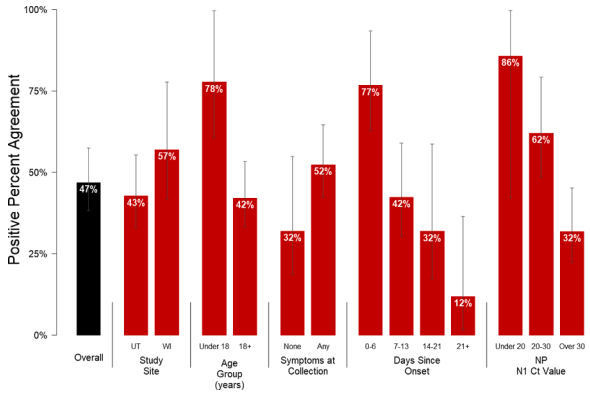

Fig. 1. Positive Percent Agreement of Single-Nostril Nasal Swab compared with Nasopharyngeal Specimen of People Enrolled in Household SARS-CoV-2 Transmission Investigations in Utah and Wisconsin, March 22–April 25, 2020
*NP: Nasopharyngeal specimen; N1 Ct: Cycle Threshold for the viral N1 target; UT: Utah; WI: Wisconsin. Error bars indicate 95% confidence intervals. Results for each subgroup, as well as N2 target cycle thresholds, are presented in Supplementary Table S2.

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